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Leukaemia Section
Short Communication

t(11;19)(q23;p13) KMT2A/SH3GL1

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Abstract

Review on t(11;19)(q23;p13) KMT2A/SH3GL1, with data on clinics, and the genes implicated.

Identity

Note
At least three other translocation t(11;19) involve KMT2A: the t(11;19)(q23;p13.1) KMT2A/ELL, the t(11;19)(q23;p13.3) KMT2A/MLLT1, and the t(11;19)(q23;p13.3) KMT2A/ACER1.

Clinics and pathology

Epidemiology

Only one case to date, a 22-month-old girl with a diagnosis of acute myeloid leukemia not otherwise specified (So et al., 1997).

Genes involved and proteins

KMT2A

Location
11q23

Protein
KMT2A is better known as MLL. MLL is a transcriptional regulatory factor. MLL regulates chromatin-mediated transcription. MLL is a major regulator of hematopoesis and embryonic development, through regulation of HOX genes expression. Translocations involving MLL are associated with high-risk de novo or treatment-related acute myeloid leukemias and myelodysplastic syndromes and acute lymphoblastic leukemias (review in Huret, 2006). Mutations in MLL cause Wiedemann-Steiner syndrome (Jones et al., 2012).

SH3GL1

Location
19p13.3

Note
The gene has previously been named EEN.

Protein
The protein, named endophilin-A2, is made of 368 amino acids (aa) in isoform 1. From N-term to C-term, it contains a Bin/Amphiphysin/Rvs (BAR) domain (aa 18-249), involved in curvature of the cell membrane, a coiled-coil domain (protein-protein interactions, aa 119-227), and a SH3 domain (protein-protein interactions, aa 306-365). Endophilin-A2 is involved in clathrin-mediated endocytosis. Endophilin-A2 facilitates G1/S cell cycle transition of multiple myeloma cells (Huang et al., 2014).

Result of the chromosomal anomaly

Hybrid gene

Description
5' KMT2A - 3' SH3GL1. KMT2A exon 6 was fused to SH3GL1 exon 2.

Fusion protein

Description
1564 amino acids (1212 from KMT2A, and 352 from SH3GL1). The fusion protein retains the AT

hooks (DNA binding) and the Zinc finger CXXC-type from KMT2A fused to most of SH3GL1, including the BAR domain and the SH3 domain.

Oncogenesis

KMT2A/SH3GL1 is localized in the nucleus, while SH3GL1 is located in the cytoplasm. KMT2A/SH3GL1 may drive to aberrant transcriptional regulation. KMT2A/SH3GL1 increases HOXA7 promoter activity (Liu et al., 2004).

References

Huang EW, Xue SJ, Li XY, Xu SW, Cheng JD, Zheng JX, Shi H, Lv GL, Li ZG, Li Y, Liu CH, Chen XH, Liu H, Li J, Liu C. EEN regulates the proliferation and survival of multiple myeloma cells by potentiating IGF-1 secretion. Biochem Biophys Res Commun. 2014 May 2;447(2):271-7

Huret JL.. MLL (myeloid/lymphoid or mixed lineage leukemia). Atlas Genet Cytogenet Oncol Haematol. 2006;10(2):83-87. http://atlasgeneticsoncology.org/Genes/MLLID13.html.

Jones WD, Dafou D, McEntagart M, Woollard WJ, Elmslie FV, Holder-Espinasse M, Irving M, Saggar AK, Smithson S, Trembath RC, Deshpande C, Simpson MA.. De novo mutations in MLL cause Wiedemann-Steiner syndrome. Am J Hum Genet. 2012 Aug 10;91(2):358-64.

Liu H, Chen B, Xiong H, Huang QH, Zhang QH, Wang ZG, Li BL, Chen Z, Chen SJ.. Functional contribution of EEN to leukemogenic transformation by MLL-EEN fusion protein. Oncogene. 2004 Apr 22;23(19):3385-94.

So CW, Caldas C, Liu MM, Chen SJ, Huang QH, Gu LJ, Sham MH, Wiedemann LM, Chan LC.. EEN encodes for a member of a new family of proteins containing an Src homology 3 domain and is the third gene located on chromosome 19p13 that fuses to MLL in human leukemia. Proc Natl Acad Sci U S A. 1997 Mar 18;94(6):2563-8.

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